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EXAMINER	
CANELLA, KAREN A	
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Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No. 10/066,305	Applicant(s) Golub et al
	Examiner Karen Canella	Art Unit 1642

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3 months* MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136 (a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1) ☐ Responsive to communication(s) filed on _____.

2a) ☐ This action is FINAL. 2b) ☒ This action is non-final.

3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11; 453 O.G. 213.

Disposition of Claims

4) ☒ Claim(s) *1-9, 12-20, and 23-34* is/are pending in the application.

4a) Of the above, claim(s) *5 and 6* is/are withdrawn from consideration.

5) ☐ Claim(s) _____ is/are allowed.

6) ☒ Claim(s) *1-4, 7-9, 12-20, and 23-34* is/are rejected.

7) ☐ Claim(s) _____ is/are objected to.

8) ☐ Claims _____ are subject to restriction and/or election requirement.

Application Papers

9) ☐ The specification is objected to by the Examiner.

10) ☐ The drawing(s) filed on _____ is/are a) ☐ accepted or b) ☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11) ☐ The proposed drawing correction filed on _____ is: a) ☐ approved b) ☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12) ☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13) ☐ Acknowledgement is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a) ☐ All b) ☐ Some* c) ☐ None of:

1. ☐ Certified copies of the priority documents have been received.
2. ☐ Certified copies of the priority documents have been received in Application No. _____.
3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

*See the attached detailed Office action for a list of the certified copies not received.

14) ☐ Acknowledgement is made of a claim for domestic priority under 35 U.S.C. § 119(e).

a) ☐ The translation of the foreign language provisional application has been received.

15) ☐ Acknowledgement is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449) Paper No(s). *6*
4) ☐ Interview Summary (PTO-413) Paper No(s). _____
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other:

DETAILED ACTION

1. Acknowledgment is made of applicants election of group I, drawn to a an oligonucleotide micro array, a method of classifying a brain tumor, a method of predicting the efficacy or treating a brain tumor, a method of assigning a brain tumor sample to a treatment class, a method for evaluating drug candidates for their effectiveness in treating brain tumors, and a method for predicting tumorigenesis, all methods comprising the determination of a gene expression profile by means of detecting polynucleotides. Acknowledgment is also made of applicants further election of M64347_at as the informative gene for examination in this application. Because applicant did not distinctly and specifically point out the supposed errors in the restriction requirement, the election has been treated as an election without traverse (MPEP § 818.03(a)).

2. Claims 1, 14, 31, 32 and 33 have been amended. Claim 34 has been added. Claims 10, 11, 21 and 22 have been canceled. Claims 1-9, 12-20 and 23-34 are pending. Claims 5 and 6, drawn to non elected genes, are withdrawn from consideration. Claims 1-4, 7-9, 12-20 and 23-34 are examined on the merits.

Specification

3. The disclosure is objected to because it contains an embedded hyperlink and/or other form of browser-executable code. Please see page 6, lines 5, 12 and 20, page 37, line 16, page 38, lines 2, 7 and 15, page 39, line 10, page 40, line 6, page 41, lines 9 and 17, page 42, lines 13 and 25, page 43, line 9, page 45, lines 10, 16 and 24, page 45, lines 6, 12 and 15, and page 46, line 1. Applicant is required to delete the embedded hyperlink and/or other form of browser-executable code. See MPEP § 608.01.

4. The use of the trademark "GeneChip" has been noted in this application. It should be capitalized wherever it appears and be accompanied by the generic terminology.

Although the use of trademarks is permissible in patent applications, the proprietary nature of the marks should be respected and every effort made to prevent their use in any manner which might adversely affect their validity as trademarks.

Claim Objections

5. Claims 1-4, 7-9, 12-20 and 23-33 are objected to because of the following informalities:

(A) claims 1-4, 7-9, 12-20 and 23-33 are drawn to non-elected genes

(B) claims 12 and 13 fail to further limit claim 1, claims 24 and 25 fail to further limit claim 14, and claims 28 and 29 fail to further limit claim 26 as only the gene M64347 is being examined in this application.

Appropriate correction is required.

Claim Rejections - 35 USC § 101

6. 35 U.S.C. 101 reads as follows:

Whoever invents or discovers any new and useful process, machine, manufacture, or composition of matter, or any new and useful improvement thereof, may obtain a patent therefor, subject to the conditions and requirements of this title.

7. Claims 26-29 are rejected under 35 U.S.C. 101 because the claimed invention is directed to non-statutory subject matter. Section 706.03(a) of the M.P.E.P states that a scientific principle, divorced from any tangible structure, can be rejected as not within the statutory classes. O 'Reilly v. Morse, 56 U.S. (15 How.) 62 (1854). A process that consists solely of the manipulation of an abstract idea is not concrete or tangible. See In re Warmerdam, 33 F.3d 1354, 1360, 31 USPQ2d 1754, 1759 (Fed.Cir. 1994). See also Schrader, 22 F.3d at 295, 30 USPQ2d at 1459. Claim 26 is drawn to a method of assigning a brain tumor to a treatment class comprising the assignment of a weighted vote for a gene based on the expression level of said gene and the degree of correlation of said gene expression with class distinction, and assigning the weighted vote for said gene to a treatment outcome class to which the brain tumor sample is then assigned. The claim relies on a hypothetical model of the relationship between gene expression and class distinction, said model represented by a mathematical equation for the determination of the weighted vote, and the outcome of the method does not result in tangible result, as the assignment of a brain tumor to a treatment outcome is an abstract result. MPEP (2106) states "For such

subject matter to be statutory, the claimed process must be limited to a practical application of the abstract idea or mathematical algorithm in the technological arts. See Alappat, 33 F.3d at 1543, 31USPQ2d at 1556-57 (quoting Diamond v. Diehr, 450 U.S. at 192, 209 USPQ at 10). See also Alappat 33 F.3d at 1569, 31 USPQ2d at 1578-79 (Newman, J., concurring) ("unpatentability of the principle does not defeat patentability of its practical applications") (citing O 'Reilly v. Morse, 56 U.S. (15 How.) at 114-19). A claim is limited to a practical application when the method, as claimed, produces a concrete, tangible and useful result; i.e., the method recites a step or act of producing something that is concrete, tangible and useful. See AT &T, 172 F.3d at 1358, 50 USPQ2d at 1452. Likewise, a machine claim is statutory when the machine, as claimed, produces a concrete, tangible and useful result (as in State Street, 149 F.3d at 1373, 47 USPQ2d at 1601) and/or when a specific machine is being claimed (as in Alappat, 33 F.3d at 1544, 31 USPQ2d at 1557 (in banc)." The instant method claims recite the production of an abstract result, and therefore do not meet the requirements of 35 U.S.C. 101.

Claim Rejections - 35 USC § 112

8.The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

9. Claims 1-4, 7-9, 12-20 and 23-34 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claim 34 is rendered vague and indefinite in the recitation of FGFR3 as the only means for identifying the claimed informative gene. FGFR3 is defined by the Table 1 as being Fibroblast Growth Factor Receptor 3 being encoded by the gene described as M64347. Claims 1, 12, 13, 14, 24, 25, 26, 28, 29, 30 and 31 recite "informative gene". The elected "informative gene" for this application is M64347_at. M64347_at is a GenBank Accession number. The sequence represented by said accession number can be subjected to editing, and thus altered. Therefore, the claims are rendered indefinite as the claimed gene upon which the method claims depend is

defined by an object which is variable. The recitation of FGFR3 itself in claim 34 is also vague and indefinite as it is recognized in the art that FGFR3 has numerous isoforms due to alternative splicing of the mRNA transcript. Thus, it is unclear what polynucleotides are encompassed by the recitation of FGFR3 in claim 34.

Claims 2 and 3 recite "brain tumor type". It is unclear if this refers to the "brain tumor" as recited in the preamble of claim 1, or to the "brain tumor sub-type" as recited in section (c) of claim 1.

The recitation of "medulloblastoma sub-type" in claim 4 lacks antecedent basis in claim 3.

Claims 7 and 8 lack active method steps, as the recitation of "utilizing" does not constitute a specific method step.

Claims 1, 14 and 31 recite in section (b) the step of isolating a polynucleotide gene expression product from at east one informative gene. In section (c) the claims recite determining the gene expression [profile of at least one informative gene. It is unclear how the isolated polynucleotide of section (b) is related to the determination of the gene expression profile of section (c).

Claim 1 fails to relate the determination of the gene expression profile in section (c) with the classification of the brain tumor as recited in the preamble.

Claim 31 recites "a method for evaluating drug candidates" in the preamble, but fails to incorporate an active method step utilizing "drug candidates".

Claim 32 fails to link the result of the comparison of the samples in section (c) with the efficacy of brain tumor treatment.

Claim 33, section (c) fails to link the result of the comparison of the samples with the onset of tumorigenesis.

Claim 33 recites in section (c) the classification of samples as tumorigenic or non-tumorigenic based on the polynucleotide expression profile of section (b). However section (d) then recites the comparison of the "tumorigenic class" of the samples at various times. The recitation of "tumor class" lacks antecedent basis within the claim. Further, the outcome of section (c) and the method objective as stated in the preamble is the prediction of the onset of

tumorigenesis. However, section (c)relies on the classification of the sample as tumorigenic or non-tumorigenic and as such does not predict tumorigenesis as an event yet to occur in the future but as an event which has already occurred.

The metes and bounds of claim 26 cannot be determined without a recitation of the mathematical equation used for the determination of the weighted vote. Furthermore, it is unclear what constitutes "one of the classes of one or more genes". Further, it is unclear what encompasses "class distinction" in section (a). The claim is vague and indefinite in the recitation of "summing the votes" as referred to in the plural as it appears from section (a) that one informative gene is given a single weighted vote. It is unclear how a weighted vote from one gene is to be subjected to "summing". The claim also fails to link by an active method step the summation of the votes to the determination of "the winning class" and further fails to link by an active method step said "winning class" with a treatment outcome class.

The metes and bound of claim 27 cannot be determined. Claim 27 fails to recite how a correlation is made between gene expression values and class distinction. Further it is unclear what constitutes "class distinction", therefore, the metes and bounds of the parameter a_g cannot be determined. Claim 27 also recites "expression value in a first class and a second class". It is unclear what constitutes said first and second classes, therefore the metes and bounds of the parameter b_g cannot be determined. It is unclear how a $\log_{10}$ gene expression value differs from the $\log_{10}$ gene expression level in the sample to be tested rendering the value of x_g vague and indefinite. In addition, claim 27 recites "in the sample to be tested" in reference to the x_g value. However, neither of claims 26 or 27 are drawn to a sample to be tested; they are drawn to a method of assigning a brain tumor sample to a treatment outcome class. Therefore, the reference to "gene expression value in the sample to be tested" is vague and indefinite as the sample would already have been tested for gene expression in order to determine the weighted vote for claim 26.

10. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it

pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

11. Claim 1-4, 7-9, 12-20, 23-29 and 34 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention.

The first paragraph of 35 U.S.C. 112 states that "the specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same...". The courts have interpreted this to mean that the specification must enable one skilled in the art to make and use the invention without undue experimentation. The courts have further interpreted undue experimentation as requiring "ingenuity beyond that to be expected of one of ordinary skill in the art" (Fields v. Conover, 170 USPQ 276 (CCPA 1971)) or requiring an extended period of experimentation in the absence of sufficient direction or guidance (In re Colianni, 195 USPQ (CCPA 1977)). Additionally the courts have determined that "...where a statement is , on its face, contrary to generally accepted scientific principles", a rejection for failure to teach how to make/or use is proper (In re Marzocchi, 169 USPQ 367 (CCPA 1971)). Factors to be considered in determining whether a disclosure meets the enablement requirement of 35 U.S.C. 112, first paragraph have been described in In re Colianni, 195 USPQ 150, 153 (CCPA 1977) and have been clarified by the Board of Patent Appeals and Interferences in Ex parte Forman, 230 USPQ 546 (BPAI 1986). Among the factor are the nature of the invention, the state of the prior art, the predictability or lack thereof in the art, the amount of direction or guidance present, the presence or absence of working examples, the breadth of the claims, and the quantity of experimentation needed. The instant disclosure fails to meet the enablement requirement for the following reasons:

The claimed invention is drawn to a method of classifying a brain tumor or assigning a brain tumor to a treatment class, said methods comprising determining the expression profile of the M64347 gene. M64347 is identified in Table I as encoding the FGFR3. As was set forth in

section 9 above, the claims are indefinite in that it is not clear what molecules are encompasses within the description of M64347 or FGFR3, or what the definitions are for the parameters of claims 26 and 27.

The art teaches that FGFR3 is expressed in many areas of the brain and can be detected in a Norther blot as a 4.4 Kda transcript in addition to two higher molecular weight unspliced transcripts in the basal ganglia, caudate, putamen and thalamus from a normal individual (Thompson et al, Genomics, 1991, vol. 11, pp. 1133-1142, especially page 1136, under the heading "Expression of FGF3"). In situ hybridization to tissue sections indicates binding of a probe at high levels to the caudate, putamen, ventral mesencepehelon, the nucleus ruber, the substantia nigra, the frontal cortex , spinal cord gray matter, and Purkinje cells.

Abbass et al (Journal of Clinical Endocrinology and Metabolism, 1997, Vol. 82, pp. 1160-1166) teaches that all pituitary adenomas expressed FGFR3, isoform I, no pituitary tumor expressed only FGFR3, isoform K, and numerous tumors had a secretable form of FGFR3, in contrast with the normal pituitary gland which expressed both isoforms of FGFR3. Abbass et al teaches that there was no correlation between the expression profile of the FGFR and tumor type, size, or aggressiveness (abstract, second column, lines 16 and 17).

Wren et al (American Journal of Human Genetics, 2000, Vol. 67, pp. 345-356 identifies M64347 as a gene having allelic diversity within the human population (page 355, second column, line 11 under the heading "Electronic-Database Information", and page 346, under the listing for Human novel growth factor receptor). It is noted that another name for the protein encoded by M64347 is "Novel Growth Factor Receptor" as evidenced by Mack (U.S. 6,303,301) (Figure 10E, line 23). Wren et al teach that polymorphic repeats within transcribed sequences represent potentially large set of disease causing loci.

The specification mentions M64347 twice: once in Table 1 which has the heading "Markers Upregulated in High Risk, Downregulated in Low Risk", and once in Figure 3C, which appears to correlate the lowered expression of M64347 with a C1 group of "survivors". The scale at the bottom of figure 3C sets the dark blue color as between minus 2 and minus three standard deviations from the mean. The brief Description of the figures indicates that figure 3C

lists fifty genes associated with treatment failure in Medulloblastoma. There are no teachings in the specification to correlate a value which is several standard deviations from the mean with a method of classifying a brain tumor or a method of predicting the efficacy of a brain tumor. Firstly the specification does not teach whether the expression of the M64347 as shown in figure 3C was obtained from the brain tumor before treatment or after treatment. Secondly, it is unclear if the lowered expression of M64347 in the C1 and C0 survivor group is indicative or predictive of a treatment failure or a treatment success as the title of figure 3C seems to be "Markers of treatment Failure" but the heading in Table 1 indicates that M64347 is in the category of "markers downregulated with low risk". Thirdly, the specification does not teach define how the C1 or C0 groups were differentiated, nor does the specification actually teach what constitutes a treatment failure or success, in terms of disease free survival or length of survival.

In reference to claims 2-4 and 15-17, the specification does not teach how the expression profile of M64347 can be correlated with a brain tumor subtype of rhabdoid tumor, primitive neuroectodermal tumor, pineoblastoma and glioblastoma as no data is presented regarding the presence or absence of M 64347 within these tumors.

There is no guidance for a specific polynucleotide probe and hybridization conditions to be used in the determination of an expression profile. It is noted that Abbass et al teach multiple isoforms for the FGFR3 gene as well as the presence of unspliced mRNA in brain tumors. Wren et al teach that the M64347 gene actual contains polymorphisms that potential can render it disease causing. It is obvious that an oligomer derived from M64347 could hybridize to any number of the polymorphic gene products or splice variants or alleles of M64347 as a function of its particular sequence. The specification provides no teachings as to the exact nature of the probe used for the expression profile, thus it cannot be construed from the specification which polymorphic variants, splice variants or alleles are integral to the claimed invention. Given these teachings and the lack of teaching in the specification regarding a specific probe and hybridization conditions for the determination of an expression profile of M64347, one of skill in the art would be subject to undue experimentation as the specific gene product referred to in the claims is undefined and further as the specification does not address the use of the M64347 gene for the

classification of a brain tumor as medulloblastoma, rhabdoid tumor, primitive neuroectodermal tumor, pinoeblastom and glioblastoma.

In the case of claims 26-29, as the specification does not define the parameters needed to calculate weighted vote for M64347, therefore the specification is not enabling for said claims. The specification seems to rely on information available at *http:// www.genome.wi.mit.edu* as opposed to an enabling disclosure. However, this does not fulfill the requirements of 35 U.S.C. 112, first paragraph.. A disclosure in an application, to be complete, must contain such description and details as to enable any person skilled in the art or science to which the invention pertains to make and use the invention as of its filing date. In re Glass, 492 F.2d 1228, 181 USPQ 31(CCPA 1974). While the prior art setting may be mentioned in general terms, the essential novelty, the essence of the invention, must be described in such details, including proportions and techniques, where necessary, as to enable those persons skilled in the art to make and utilize the invention. Specific operative embodiments or examples of the invention must be set forth. An application as filed must be complete in itself in order to comply with 35 U.S.C. 112. Material nevertheless may be incorporated by reference, Ex parte Schwarze, 151 USPQ 426 (Bd. App. 1966). An application for a patent when filed may incorporate "essential material" by reference to (1) a U.S. patent, (2) a U.S. patent application publication, or (3) a pending U.S. application, subject to the conditions. "Essential material" is defined as that which is necessary to (1) describe the claimed invention, (2) provide an enabling disclosure of the claimed invention, or (3) describe the best mode (35 U.S.C. 112). In any application which is to issue as a U.S. patent, essential or non-essential material may not be incorporated by reference to hyperlinks. See MPEP ° 608.01.

Claim Rejections - 35 USC § 102

12. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless -

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

13. Claim 30 is rejected under 35 U.S.C. 102(b) as being anticipated by Levine et al (WO 99/50456). Claim 30 is drawn in part to an oligonucleotide microarray having immobilized thereon an oligonucleotide probe specific for M64347. Levine et al disclose an oligonucleotide array for determining the expression levels of relevant genes, including gene #32 (figure 1B) which is described as the M64347 gene (page 5, lines 17-22, page 6, lines 6-18, page 7, lines 14-20).

14. Claim 32 and 33 are rejected under 35 U.S.C. 102(e) as being anticipated by either of Au-Young et al (U.S. 6, 500, 938) or Friend et al (U.S. 6,218,122).

Claim 32 is drawn to a method for monitoring the efficacy of a brain tumor treatment comprising obtaining, at various times, samples of cells from a patient; determining the polynucleotide expression profile of the sample; classifying the samples for treatment outcome based on the expression profile; and determining the efficacy of the brain tumor treatment by comparing the treatment outcome class of the samples at various time points. Claim 33 is drawn to a method comprising obtaining, at various times, samples of cells from a patient; determining the polynucleotide expression profile of the sample; classifying the samples as tumorigenic or non-tumorigenic based on the expression profile, and determining the onset of tumorigenesis by comparing the tumorigenic class of the samples at various times.

Au-Young et al disclose a method for monitoring the progression of a disease or the efficacy of a treatment comprising detecting an expression profile by means of a microarray (column 11, line 15 to column 12, line 67). As Au-Young et al specifies the monitoring of diseases, it is inherent that samples are obtained from patients being treated at various time points. Further, the detection of cancer as disclosed by Au-Young appears to be identical to the "prediction of tumorigenesis" as claimed. Au-Young et al disclose cancers of the brain as a specific embodiment (column 11, lines 11-12).

Friend et al disclose a method for detecting changes in a biological state of a subject which are correlated to one or more disease states and methods for monitoring the efficacies of a therapy or therapies upon a subject, said methods comprising the determination of an expression profile from said cells in said patient (column 3, lines 7-49, column 9, lines 1-19). Friend et al disclose glioma, astrocytoma, medulloblastoma, craniopharyngioma, ependymoma, pinealoma, oligodendroglioma, meningioma and neuroblastoma (column 8) and medullary carcinoma (column 7) as diseases encompassed by the invention, thus fulfilling the specific embodiment of brain cancer (Table I). As Friend et al disclose the detection of changes in a biological state, the specific embodiments of claim 33 with respect to detecting the onset of tumorigenesis are fulfilled. Further, by the same logic, as Friend et al disclose a method of monitoring the efficacy of a therapy the specific embodiment of claim 33 with respect to obtaining cells at various time points obtained from a patients are inherent within the method, as the act of monitoring encompasses sampling over time.

Claim Rejections - 35 USC § 103

15. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

16. Claim 31 is rejected under 35 U.S.C. 103(a) as being unpatentable over Au-Young et al (U.S. 6,500,938) in view of Abbass et al (Journal of Clinical Endocrinology and Metabolism, 1997, Vol. 82, pp. 1160-1166). Claim 31 is drawn to a method for evaluating drug candidates for their effectiveness in treating brain tumors comprising obtaining a sample of cells derived for a brain tumor and correlating the expression profile of M64347 with the effectiveness of the drug candidate in the treatment of brain tumors.

Au-Young et al teach methods for monitoring disease states, including brain cancer, and therapies thereof using an expression profile for the reasons set forth above. . Au-Young et al teach that the methods can be used for monitoring the efficacy of treatment and can also be used to generate expression profiles of therapeutic agents and that this can allow for the rapid screening of large numbers of drug candidates to find ones that have the same expression profile as known therapeutic agents (column 11, lines 50-59 and column 12, lines 42-58). Au-Young et al do not teach the expression profile of M64347 or the FGFR3 encoded thereby.

Abbass et al teach that the expression of the mRNA encoding the secreted form of FGFR3 is correlated with pituitary adenomas.

It would have been *prima facia* obvious to one of ordinary skill in the art at the time the claimed invention was made to use the expression profile of the secreted form of FGFR3 in the method for evaluating drug candidates for their effectiveness in treating brain tumors.

One of ordinary skill in the art would have been motivated to do so with a reasonable expectation of success by the teachings of Abbass et al on the unique expression of the secretable form of FGFR3 mRNA in pituitary adenomas versus the lack of expression of the secretable form of this receptor in normal pituitary. One of skill in the art would be motivated to use polynucleotide encoding said secretable receptor in a method for evaluating drug candidates, as lack of expression of said polynucleotide would indicate that the samples of cells were exhibiting gene expression consistent with a normal pituitary gland and the attainment of a normal phenotype, and increase or no change in the expression of said polynucleotide would indicate that the drug did not have efficacy as the sample of cells was expressing a polynucleotide indicative of tumorigenic cells.

17. All claims are rejected.

Conclusion

18. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Karen Canella whose telephone number is (703) 308-8362. The examiner can normally be reached on Monday through Friday from 8:30 am to 6:00 pm. A message may be left on the examiner's voice mail service. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Anthony Caputa, can be reached on (703) 308-3995. Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the Group receptionist whose telephone number is (703) 308-0196.

Karen A. Canella, Ph.D.
Patent Examiner, Group 1642
January 27, 2003